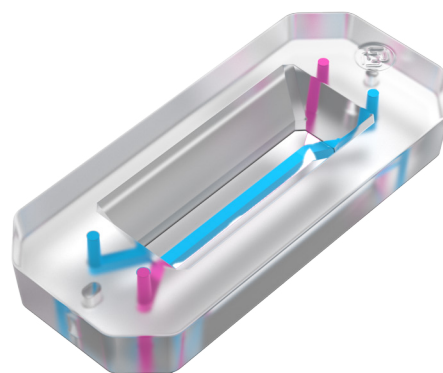


Chip-R1™ Basic Research Kit

Improve precision in ADME and Toxicology applications with a low drug-absorption profile



Overview

An Organ-Chip is a living, micro-engineered cell culture system that recreates the natural physiology and mechanical forces that cells experience within the human body. The Chip-R1™ Rigid Chip was designed to minimize drug absorption and enhance biological modeling by using low-drug-absorbing materials and featuring increased shear stress in the vascular channel. Constructed using rigid plastics, including a polycarbonate tissue culture membrane, Chip-R1 builds upon the foundation of microfluidic Organ-Chips, offering researchers greater precision in predicting human drug responses. With the Emulate Chip-R1 Basic Research Kit, users can build a wide variety of non-stretch organ models for ADME and toxicology applications without the concern of compound absorption by the microfluidic system.

Kit Components

The Chip-R1 Basic Research Kit contains all the non-biological components required to create an Organ-Chip for the [Human Emulation System](#). Each kit consists of Chip-R1 Rigid Chip consumables, chip carriers, and Pod® Portable Modules (**Figure 1**). Chip carriers securely connect the chips to the Pods, while the Pod reservoir lid acts as the interface between [Zoë](#) and the chip.

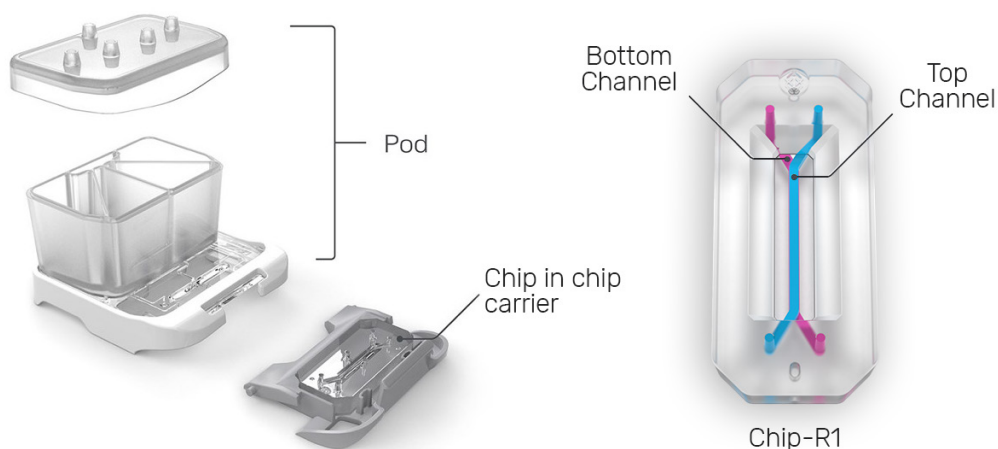


Figure 1: Chip-R1 Basic Research Kit Components.

Chip-R1 Configuration

The Chip-R1 Rigid Chip (**Figure 2**) is made of rigid plastics that minimize compound absorption. Chip-R1 retains much of the same microfluidic architecture of the Chip-S1® Stretchable Chip, including co-culture to model the tissue-tissue interface, independent perfusion of the apical and basal channels, and compatibility with Emulate’s instrumentation hardware. With a polycarbonate tissue culture membrane, Chip-R1 is better suited for organ models that do not require mechanical stretch to mimic physiologically relevant strains cells experience *in vivo*—like peristalsis in the intestine or inflation of the lungs—such as liver and kidney.

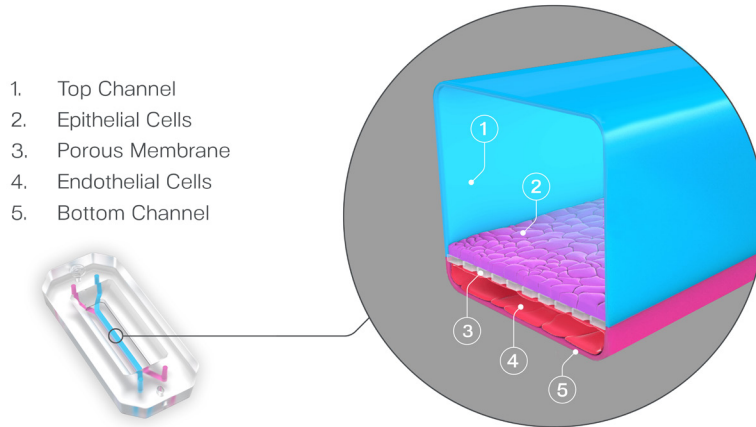


Figure 2: Chip-R1 diagram.

Pod Portable Module

Each Chip-R1 connects to a Pod-2™ which, through Zoë, enables automated control of media flow and dosing while maintaining ease of portability for routine microscopy observation (see **Figure 3**). The Pod stores 4 mL of media for each microfluidic channel, enabling automated media flow for up to five days. Media effluent can be easily collected from the outlet reservoirs for downstream analysis.

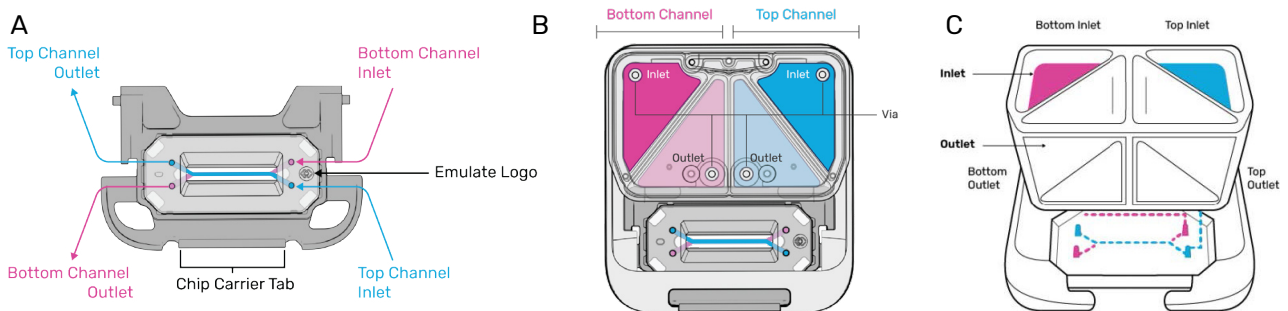


Figure 3: **A)** Chip carrier diagram showing direction of fluid flow through the chip. **B)** Pod diagram showing reservoirs for top and bottom channel inlets and outlets. **C)** Diagram demonstrating fluid flow between Pod and chip.

Drug Absorption Characterization of Chip-R1

Many microphysiological systems (MPSs), including Organ-Chips, are made with polydimethylsiloxane (PDMS) due to its beneficial properties such as transparency, flexibility, biocompatibility, and oxygen permeability. However, this material is known to absorb a subset of small hydrophobic molecules, which can interfere with the assessment of drug efficacy, toxicity, and ADME. Chip-R1 overcomes these limitations by using non-drug-absorbing rigid plastics, ensuring greater accuracy for evaluating drug candidates while building on key microfluidic capabilities.

To characterize the improvement in mitigating compound absorption, a panel of eight compounds was tested on both Chip-R1 and Chip-S1 chips. These compounds were selected for their relevance to hepatotoxicity or liver metabolism functions as well as for their range of physiochemical properties (**Table 1**), including hydrophobicity (logP), molecular weight, and topological surface area.

Compound	Dosing concentration	logP	Molecular Weight (Da)	Topological Polar Surface Area (Å ²)	pKa	Ionization status at pH 7.4
Nefazodone	30 µM	4.3 - 4.7	470	51.6	7.09	Neutral
Diclofenac sodium	20 µM	4.26 - 4.75	318.1	52.2	4	Anionic
Bufuralol HCl	10 µM	2.99 - 3.24	297.82	45.4	13.06	Cationic
Midazolam	20 µM	2.73	325.8	30.2	5.5	Neutral
Labetalol	137 µM	2.7 - 3.1	328.4	95.58	9.3	Cationic
S-mephenytoin	35 µM	1.64 - 1.69	218.3	49.4	8.1	Neutral
Phenacetin	30 µM	1.41 - 1.62	179.2	38.3	14.98	Neutral
Trovafloxacin	200 µM	0.3 - 0.9	416.4	99.8	5.9	Zwitterion

Table 1: Compounds assessed for absorption on Chip-S1 and Chip-R1.

These compounds were applied to either the top or bottom channels of acellular Chip-S1 and Chip-R1 consumables at a flow rate of 30 µL/h. To determine the average compound recovery after 24 hours, effluent was collected from Pod reservoirs (inlets and outlets) for the 24–28 hour exposure interval, since a four-hour time interval was required to provide sufficient volume for LC/MS analysis. Compound recovery is reported as the average recovery for the four-hour time interval and represented as a ratio of Pod outlet concentration to Pod inlet concentration (**Figure 4**).

Drug Absorption Characterization of Chip-R1 (Continued)

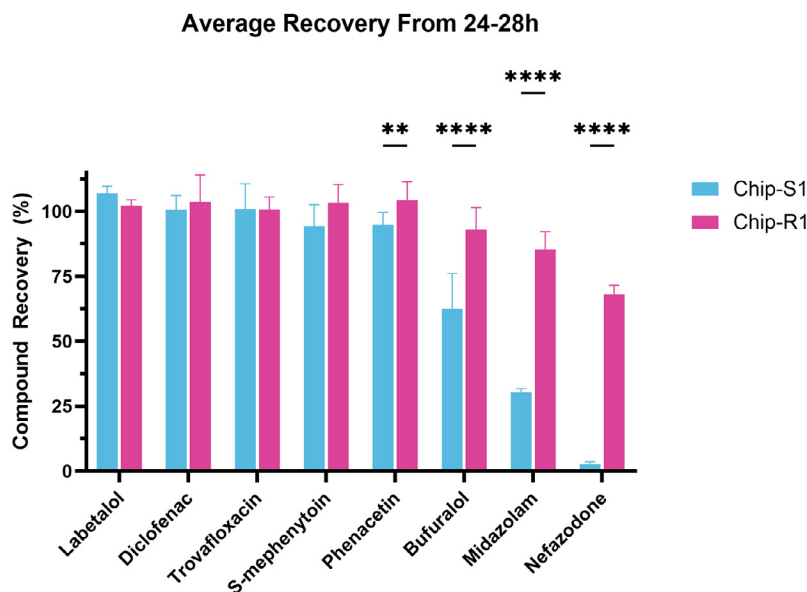


Figure 4: Average Compound Recovery Between 24–28 Hours of Flow. Data shown as mean \pm . Significance in recovery determined by two-way ANOVA with Fisher's LSD multiple comparison test. $n=3-4$ chips per condition, with values for top and bottom channels average per chip, ** $p<0.01$, $p<0.0001$. assessed for absorption on Chip-S1 and Chip-R1.

Out of the eight compounds tested, three demonstrated high absorption on Chip-S1: Nefazodone, Bufuralol, and Midazolam. These compounds would be predicted to have PDMS absorption liability based on their relatively high hydrophobicity, low molecular weight, and low topological polar surface area. Chip-R1 demonstrated a significantly improved recovery profile of PDMS-liable compounds after 24 hours versus Chip-S1:

- Bufuralol improved from 60% to 93% recovery
- Midazolam improved from 25% to 85% recovery
- Nefazodone improved from 2.7% to 68% recovery

The remaining compounds tested demonstrated no significant absorption on either chip.

Although Nefazodone showed an impressive improvement—with a 26-fold increase in recovery on Chip-R1 compared to Chip-S1—it is important to understand the absorption kinetics on Chip-R1 for compounds that still show some absorption liability. Thus, with Nefazodone being the most prone to absorption from the set of compounds tested, a more in-depth time course analysis was performed to better understand its absorption behavior in Chip-R1. As shown in **Figure 5**, Chip-S1 demonstrated negligible recovery of Nefazodone over the course of 48 hours, indicating that the PDMS-based chip absorbed most of the compound for the duration of treatment. While Chip-R1 demonstrated low recovery rates within the first few hours of dosing, after 48 hours, the rate of recovery was greater than 80% on average across both top and bottom channels. Extrapolated out to 72 hours, one would expect to see >90% recovery of Nefazodone. Together, these datasets demonstrate Chip-R1's utility in ADME and toxicology applications, even for compounds that are highly prone to PDMS absorption such as Nefazodone.

Drug Absorption Characterization of Chip-R1 (Continued)

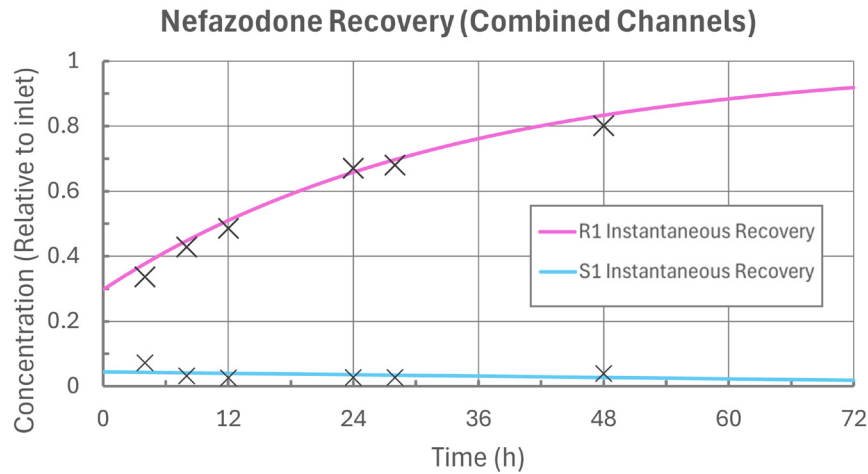


Figure 5: Absorption kinetics of Nefazodone on Chip-R1 versus Chip-S1. Compound recovery was calculated by taking the ratio of outlet to inlet concentration. Marked X's denote measured data averaged over a four-hour time interval. Solid lines represent curve fit for instantaneous recovery values. $n=3-4$ chips per condition.

Additional Features and Benefits

More Physiologically Representative Modeling

The unique features of Chip-R1 can improve research in areas beyond ADME and toxicology. Chip-R1 features a shorter bottom channel height at only $100\ \mu\text{m}$ tall, which in conjunction with a maximum flow rate of $2,000\ \mu\text{L/h}$, enables researchers to achieve a maximum shear stress of $2.3\ \text{dyn/cm}^2$. The modified design of the vascular channel enables physiologically relevant levels of shear stress to be applied, which is critical for applications such as immune cell recruitment. Additionally, Chip-R1 features a thinner membrane at just $22\ \mu\text{m}$ thick with $3\ \mu\text{m}$ pores, enabling enhanced cellular crosstalk and better approximation of the *in vivo* milieu.

Shorter Imaging Distance to the Top Channel

Chip-R1 features a distance of only $172\ \mu\text{m}$ from the bottom of the chip to the top of the tissue culture membrane, thus requiring a significantly shorter working distance to reach the epithelial layer (**Figure 6**).

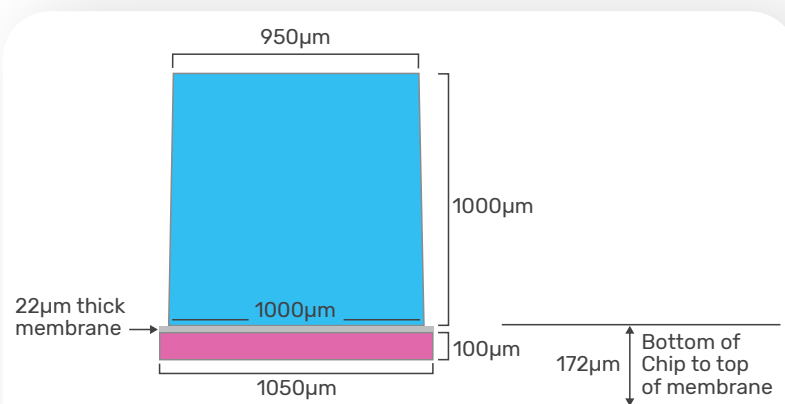


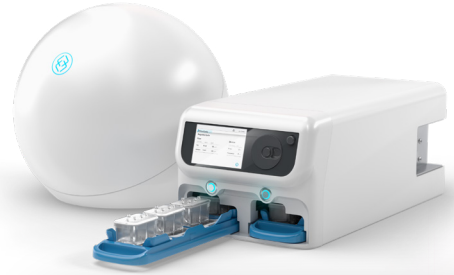
Figure 6: Cross-sectional diagram of Chip-R1 illustrating imaging distance required to reach the top channel.

Part of the Human Emulation System®

The Emulate Chip-R1 Basic Research Kit is designed to be used as part of the Human Emulation System, a complete Organ-on-a-Chip solution that includes instruments, consumables, and software, providing the dynamic conditions needed to culture up to 12 Organ-Chips per Zoë Culture Module.

In addition to the Chip-R1 Basic Research Kit, Emulate offers additional companion products:

- Pod Imaging Adapter: for microscopic inspection during an experiment
- Fixed Chip Imaging Adapter: for post-experiment fixation, staining, and analysis



Chip Specifications:

Top Channel

Width x height dimensions	1,000 μm x 1,000 μm
Area at membrane	26.66 mm^2
Channel volume	24.52 μL
Imaging distance from bottom of chip to top of membrane	172 μm

Bottom Channel

Width x height dimensions	1,050 μm x 100 μm
Area at membrane	29.46 mm^2
Volume	2.97 μL

Membrane

Pore diameter	3.0 μm
Pore spacing	Random distribution (Track-etched membrane)
Porosity	2.8%
Thickness	22 μm

Kit Specifications:

Specification

Details

Compatible cell types

The open nature of the Emulate Chip-R1 Basic Research Kit makes it compatible with practically any type of human or animal cells, including:

- Primary cells
- Dissociated organoids
- Induced pluripotent stem cells (iPSCs)
- Immortalized cell lines

Due to the rigid nature of the consumable, Chip-R1 is not recommended for organ models that require stretch.

Characterization endpoints

Image analysis

- Brightfield and fluorescence microscopy
- Omics analysis
- RNAseq, proteomics, and metabolomics
- Effluent analysis
- Cytokine release, injury markers, barrier function (P_{app}), etc.

Storage conditions

Ambient temperature (15–25°C)

Shelf life

1 year from date of manufacture

Sterility

All consumables—including chips, Pods, and carriers—are sterilized prior to shipment.

Zoë Culture Module Firmware Requirements:

Using Chip-R1 with your Zoë Culture Module may require upgrading your Zoë's firmware. Please refer to the chart below to determine whether your system will require a firmware upgrade prior to running Chip-R1 experiments.

Zoë Device	Chip R1 Version Info	Upgrade Path
Zoë-CM1®	Display Firmware: 1.3.2 Core Firmware: 1.2.5	Any Zoë-CM1 user can upgrade their Zoë display and core firmware using Utility Hub 1.0 software from the Emulate website .
Zoë-CM2®	Display Firmware: 1.3.2 Core Firmware: 1.4.5	Firmware 1.3.2: Any user with a Zoë-CM2 running this version of firmware can self-upgrade using Utility Hub 1.0 software from the Emulate website . Below firmware 1.3.2: Any user with a Zoë-CM2 with a version of firmware below 1.3.2 cannot self-update. Please contact Emulate Support (support@emulatebio.com) for further assistance.

Ordering Information

Kits are available in sets of 12 or 24 chips. Each set contains:

- 1 Chip-R1 Rigid Chip in a chip carrier
- 1 Pod Portable Module

Product Name	Kit Contents	Catalog Number
Chip-R1 Starter Pack (6-pack)	6 sets of chips, 2 Chip Cradles, 10 square Petri dishes, plus 4 Steriflip® filters	STP-R1-6
Chip-R1 Basic Research Kit (12-pack)	12 sets of chips, plus 6 Steriflip® filters	BRK-R1-12
Chip-R1 Basic Research Kit (24-pack)	24 sets of chips, plus 8 Steriflip® filters	BRK-R1-24

Companion Products:

Product Name	Kit Contents	Catalog Number
Pod Imaging Adapter	Organizes 2 Pods for quick cell viability and health checks and ensures compatibility with SBS footprint inverted microscopes	POD-IMG
Fixed Chip Imaging Adapter	Organizes 12 fixed chips for high-throughput imaging and ensures compatibility with SBS footprint imaging equipment	CHIP-IMG